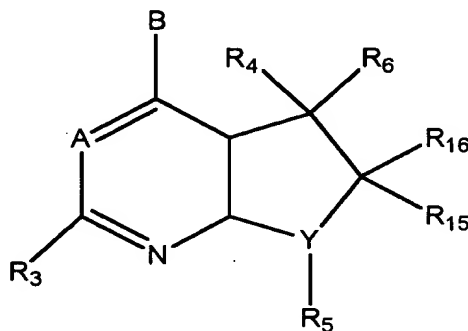


21
This application is a continuation in part of Serial Number 08/741,066 filed on October 30, 1996 (now issued as Patent No 6,403,599) which claims benefit of 60/006,333 filed November 8, 1995, and also is a continuation in part of application Serial No 09/254,387 filed March 4, 1999 (now issued as Patent No 6,316,631) which is the United States part of International Patent Application PCT/IB95/00437 which was filed on June 6, 1995

IN THE CLAIMS

Please amend claims 1,2, 3 4, 14 and 15 to read as follows:

1(Amended) A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is -CR₇ or N;

B is -NR₁R₂, -CR₁R₂R₁₁, -C(=CR₂R₁₂)R₄, -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₂OR₁, -CHR₁OR₂, -CHR₂SR₁, -C(S)R₂, -C(O)R₂, -CHR₂NR₁R₂, -CHR₁NHR₂, -CHR₁N(CH₃)R₂, or -NR₁₂NR₁R₂;

Y is CH or N;

22
R₁ is C(O)H, C(O)(C₁-C₆ hydrocarbyl), C(O)(C₁-C₆ hydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C(O)(C₃-C₈ cyclohydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C(O)(C₁-C₆ hydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), -C(O)(C₃-C₈ cyclohydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), C₁-C₆ hydrocarbyl, C₃-C₈ cyclohydrocarbyl, C₄-C₈ heterocyclohydrocarbyl, -(C₁-C₆ hydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C₃-C₈ cyclohydrocarbylene)(C₃-C₈ cyclohydrocarbyl), -(C₁-C₆ hydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), -(C₃-C₈ cyclohydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), or -O-aryl, or -O-(C₁-C₆ hydrocarbylene)-aryl; wherein said aryl, C₄-C₈ heterocyclohydrocarbyl, C₁-C₆ hydrocarbyl, C₃-C₈ cyclohydrocarbyl, C₃-C₈ cyclohydrocarbylene, and

C₁-C₆ hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R₈ independently selected from the group consisting of C₁-C₄ hydrocarbyl, -C₃-C₈ cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF₃, -O-(C₁-C₆ hydrocarbyl), -O-(C₃-C₈ cyclohydrocarbyl), -O-CO-(C₁-C₄ hydrocarbyl), -O-CO-NH(C₁-C₄ hydrocarbyl), -O-CO-N(R₂₄)(R₂₅), -N(R₂₄)(R₂₅), -S(C₁-C₄ hydrocarbyl), -S(C₃-C₈ cyclohydrocarbyl) -N(C₁-C₄ hydrocarbyl)CO(C₁-C₄ hydrocarbyl), -NHCO(C₁-C₄ hydrocarbyl), -COO(C₁-C₄ hydrocarbyl), -CONH(C₁-C₄ hydrocarbyl), -CONC₁-C₄ hydrocarbyl(C₁-C₂ hydrocarbyl), CN, NO₂, -OSO₂(C₁-C₄ hydrocarbyl), S⁺(C₁-C₆ hydrocarbyl)(C₁-C₂ hydrocarbyl), -SO(C₁-C₄ hydrocarbyl) and -SO₂(C₁-C₄ hydrocarbyl); and wherein the C₁-C₆ hydrocarbyl, C₁-C₆ hydrocarbylene, C₅-C₈ cyclohydrocarbyl, C₅-C₈ cyclohydrocarbylene, and C₅-C₈ heterocyclohydrocarbyl moieties of R₁ may optionally independently contain from one to three double or triple bonds; and wherein the C₁-C₄ hydrocarbyl moieties and C₁-C₆ hydrocarbyl moieties of R₈ can optionally independently be substituted with hydroxy, amino, C₁-C₄ alkyl, aryl, -CH₂-aryl, C₃-C₅ cycloalkyl, or -O-(C₁-C₄ alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R₁ contains from one to three heteromoieties selected from oxygen, S(O)_m, nitrogen, and NR₁₂;

R₂ is hydrogen, C₁-C₁₂ hydrocarbyl, C₃-C₈ cyclohydrocarbyl, C₄-C₈ heterocyclohydrocarbyl, -(C₁-C₆ hydrocarbylene)(C₃-C₈ cyclohydrocarbyl), -(C₃-C₈ cyclohydrocarbylene)(C₃-C₈ cyclohydrocarbyl), -(C₁-C₆ hydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), -(C₃-C₈ cyclohydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), aryl, -(C₁-C₆ hydrocarbylene)aryl, or -(C₃-C₈ cyclohydrocarbylene)(aryl); wherein each of the foregoing R₂ groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C₁-C₆ alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C₁-C₆ alkoxy, -OH, -O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), -S(O)(C₁-C₆ alkyl), -S(O)₂(C₁-C₆ alkyl), S⁺(C₁-C₆ alkyl)(C₁-C₂ alkyl)I', CN, and NO₂; and wherein the C₁-C₁₂ hydrocarbyl, -(C₁-C₆ hydrocarbylene), and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms of R₂ may optionally independently contain from one to three double or triple bonds; and wherein each heterocyclohydrocarbyl group of R₂ contains from one to three heteromoieties selected from oxygen, S(O)_m, nitrogen, and NR₁₂;

or when R_1 and R_2 are as in $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_1R_2$ or $-NR_1R_2$, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12} ; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3 , $-O-(C_1-C_4 \text{ alkyl})$, $-O-CO-(C_1-C_4 \text{ alkyl})$, $-O-CO-NH(C_1-C_4 \text{ alkyl})$, $-O-CO-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-NH(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})CO(C_1-C_4 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, CN , NO_2 , $-OSO_2(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, and $-SO(C_1-C_4 \text{ alkyl})$, wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3 , NH_2 , $NH(C_1-C_2 \text{ alkyl})$, $N(CH_3)_2$, $-NHCOCF_3$, $-NHCH_2CF_3$, $S(O)_m(C_1-C_4 \text{ alkyl})$, $CONH_2$, $-CONHCH_3$, $CON(CH_3)_2$, $-CF_3$, or CH_2OCH_3 ;

R_4 is hydrogen, C_1 - C_4 hydrocarbyl, C_3 - C_5 cycloalkyl, $-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_5 \text{ cycloalkyl})$, $-(C_3-C_5 \text{ cycloalkylene})(C_3-C_6 \text{ cycloalkyl})$, cyano, fluoro, chloro, bromo, iodo, $-OR_{24}$, C_1 - C_6 alkoxy, $-O$ -cycloalkyl, $-O-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_5 \text{ cycloalkyl})$, $-O-(C_3-C_5 \text{ cycloalkylene})(C_3-C_5 \text{ cycloalkyl})$, $-CH_2SC(S)O(C_1-C_4 \text{ alkyl})$, CH_2OCF_3 , CF_3 , amino, nitro, $-NR_{24}R_{25}$, $-(C_1-C_4 \text{ hydrocarbylene})-OR_{24}$, $-(C_1-C_4 \text{ hydrocarbylene})Cl$, $-(C_1-C_4 \text{ hydrocarbylene})NR_{24}R_{25}$, $-NHCOR_{24}$, $-NHCONR_{24}R_{25}$, $-CH=NOR_{24}$, $-NHNOR_{24}R_{25}$, $-S(O)_mR_{24}$, $-C(O)R_{24}$, $-OC(O)R_{24}$, $-C(O)CN$, $-C(O)NR_{24}R_{25}$, $-C(O)NHNOR_{24}R_{25}$, and $-COOR_{24}$, wherein the hydrocarbyl and hydrocarbylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCH_3$, $-NHCOCH_2Cl$, $-NH(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-CO(C_1-C_4 \text{ alkyl})$, C_1 - C_6 alkoxy, C_1 - C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1 - C_{10} hydrocarbyl, $-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_1-C_4 \text{ hydrocarbylene})(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkyl})$, $-(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_4-C_8 \text{ heterocycloalkyl})$, C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CON(OR_{22})R_{23}$, $-CO_2R_{26}$, $-C=N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1 - C_{10} alkyl, C_3 - C_8 cycloalkyl, $(C_1-C_4 \text{ hydrocarbylene})$, $(C_3-C_8 \text{ cycloalkyl})$, $(C_3-C_8 \text{ cycloalkylene})$, and $(C_4-C_8$

heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected from C_1 - C_4 alkyl, C_3 - C_8 cycloalkyl, $(C_1$ - C_4 hydrocarbylene)(C_3 - C_8 cycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), C_1 - C_4 haloalkyl, hydroxy, C_1 - C_6 alkoxy, nitro halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26} , $-CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R_5 , which ring optionally can contain one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any $-S-S-$, $-O-O-$, $-S-O-$, or $-N-S-$ bonds, and which ring is optionally substituted with C_1 - C_4 alkyl, C_3 - C_8 cycloalkyl, $-(C_1$ - C_4 alkylene)(C_3 - C_8 cycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), C_1 - C_4 haloalkyl, nitro, halo, cyano $-NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26} , $-CO(NOR_{26})R_{25}$, or $-S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27} , can further be selected from $-SO_2NH(C_1$ - C_4 alkyl), $-SO_2NH(C_1$ - C_4 alkylene)(C_3 - C_8 cycloalkyl), $SO_2NH(C_3$ - C_8 cycloalkyl), $-SO_2NH(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-SO_2NH_2$, $-NHSO_2(C_1$ - C_4 alkyl), $-NHSO_2(C_3$ - C_8 cycloalkyl), $-NHSO_2(C_1$ - C_4 alkylene)(C_3 - C_8 cycloalkyl), and $-NHSO_2(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl); and wherein the hydrocarbyl, and hydrocarbylene groups of R_5 may independently optionally contain one double or triple bond; R_6 is hydrogen, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, $-(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl), or $-(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or R_6 and R_4 can together form an oxo ($=O$) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO_m , N, and NR_{12} , but not containing any $-O-O-$, $-S-O-$, $-S-S-$, or $-N-S-$ bonds, and further optionally substituted with C_1 - C_4 hydrocarbyl or C_3 - C_6 cycloalkyl, wherein said C_1 - C_4 hydrocarbyl substituent may optionally contain one double or triple bond;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, $-O(C_1$ - C_2 alkyl), $-O$ (cyclopropyl), $-COO(C_1$ - C_2 alkyl), $-COO(C_3$ - C_8 cycloalkyl), $-OCF_3$, CF_3 , $-CH_2OH$, or CH_2OCH_3 ;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or C_1 - C_4 alkyl;

R_{16} and R_{17} are each, independently, hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that R_{16} and R_{17} are not both methoxy or ethoxy;

or R_{16} and R_{17} together form an oxo ($=O$) group;

or R_{16} and R_{17} are connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing from one to three heterologous ring members selected from O, SO_m , N, and NR_{12} , but not containing any $-O-O-$, $-S-O-$, $-S-S-$, or $-N-S-$

bonds, and further optionally substituted with C₁-C₄ hydrocarbonyl or C₃-C₆ cycloalkyl, wherein said C₁-C₄ hydrocarbonyl substituent may optionally contain one double or triple bond;

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄ alkylene)(C₃-C₈ cycloalkyl);

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₁₄ alkyl, C₁-C₁₄ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄ alkylene)(C₃-C₈ cycloalkyl);

R₂₃ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, -(C₁-C₄ alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

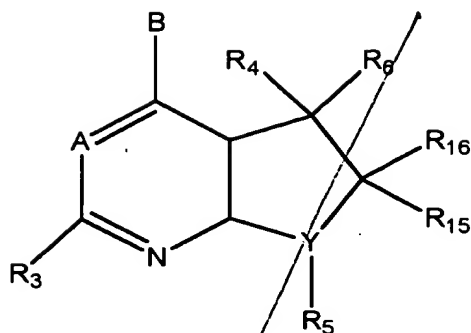
R₂₄ and R₂₅ are independently at each occurrence selected from hydrogen, -C₁-C₄ alkyl, C₁-C₄ haloalkyl, -(C₁-C₄ alkylene)OH, -(C₁-C₄ alkylene)-O-(C₁-C₄ alkyl), -(C₁-C₄ alkylene)-O-(C₃-C₈ cycloalkyl), C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -C₄-C₈ heterocyclohydrocarbonyl, -(C₁-C₄ alkylene)(C₄-C₈ heterocyclohydrocarbonyl), aryl, and -(C₁-C₄ alkylene)(aryl), wherein the -C₄-C₈ heterocyclohydrocarbonyl groups can each independently optionally be substituted with aryl, CH₂-aryl, or C₁-C₄ alkyl, and can optionally contain one or two double or triple bonds; or, when R₂₄ and R₂₅ are as NR₂₄R₂₅, -C(O)NR₂₄R₂₅, -(C₁-C₄ alkylene)NR₂₄R₂₅, or -NHCONR₂₄R₂₅, then NR₂₄R₂₅ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)_m, oxygen, nitrogen, and NR₁₂, and optionally containing from one to three double bonds;

R₂₆ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, and -(C₁-C₄ alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocyclohydrocarbonyl groups of the compound of formula II, do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)_m heterologous members.

2.(Amended) A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is $-\text{CR}_7$ or N;

B is $-\text{NR}_1\text{R}_2$, $-\text{CR}_1\text{R}_2\text{R}_{11}$, $-\text{C}(=\text{CR}_2\text{R}_{12})\text{R}_1$, $-\text{NHCHR}_1\text{R}_2$, $-\text{OCHR}_1\text{R}_2$, $-\text{SCHR}_1\text{R}_2$, $-\text{CHR}_2\text{OR}_{12}$, $-\text{CHR}_2\text{SR}_{12}$, $-\text{C}(\text{S})\text{R}_2$ or $-\text{C}(\text{O})\text{R}_2$;

Y is $-\text{CH}$ or N;

R_1 is $\text{C}_1\text{-C}_6$ hydrocarbyl which may optionally be substituted with one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF_3 , $\text{C}_1\text{-C}_4$ alkoxy, $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{O}-\text{CO}-\text{NH}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{O}-\text{CO}-\text{N}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})(\text{C}_1\text{-C}_2 \text{ hydrocarbyl})$, $-\text{NH}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_4) \text{CO}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{NHCO}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{COO}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})\text{hydrocarbyl}$, $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, $-\text{CON}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, CN, NO_2 , $-\text{SO}(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$ and $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ hydrocarbyl})$, and wherein said $\text{C}_1\text{-C}_6$ hydrocarbyl and the $(\text{C}_1\text{-C}_4)\text{hydrocarbyl}$ moieties in the foregoing R_1 groups may optionally contain one carbon-carbon double or triple bond;

R_2 is $\text{C}_1\text{-C}_{12}$ hydrocarbyl, aryl or $-(\text{C}_1\text{-C}_4 \text{ hydrocarbylene})\text{aryl}$ wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $-(\text{C}_1\text{-C}_6 \text{ alkylene})\text{cycloalkyl}$, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said $-(\text{C}_1\text{-C}_6 \text{ alkylene})\text{cycloalkyl}$ having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by $\text{N}-\text{R}_9$, wherein R_9 is hydrogen or $\text{C}_1\text{-C}_4$ alkyl; and wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and $\text{C}_1\text{-C}_4$ alkyl, or with one substituent selected from bromo, iodo, $\text{C}_1\text{-C}_6$ alkoxy,

17
-O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), CN, NO₂, -SO(C₁-C₄ alkyl), and -SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ hydrocarbyl and the C₁-C₄ hydrocarbylene moiety of said -(C₁-C₄ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR₁R₂ or -CR₁R₂R₁₁ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ hydrocarbyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, trifluoromethoxy, -CH₂OCH₃, -CH₂OCH₂CH₃, -CH₂CH₂OCH₃, -CH₂OF₃, CF₃, amino, nitro, -NH(C₁-C₄ alkyl), -N(CH₃)₂, -NHCOCH₃, -NHCONHCH₃, -SO_n(C₁-C₄ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ hydrocarbyl), -CHO, cyano or -COO(C₁-C₄ alkyl) wherein said C₁-C₄ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH₃, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)₂, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, chloro, cyano and nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R₅ is substituted with from one to three substituents independently selected from fluoro, chloro, C₁-C₆ alkyl, and C₁-C₆ alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C₁-C₆ alkyl)O(C₁-C₆)alkyl, -NHCH₃, -N(CH₃)₂, -COOH, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein the C₁-C₄ alkyl and C₁-C₆ alkyl moieties of the foregoing R₅ groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R₆ is hydrogen or C₁-C₆ alkyl, wherein C₁-C₆ alkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

R₇ is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C₁-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -OCF₃, CF₃, -CH₂OH, -CH₂OCH₃ or -CH₂OCH₂CH₃;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl; and

R₁₆ and R₁₇ are each independently, hydrogen, hydroxy, ethyl, ethyl, methoxy, or ethoxy, except that R₁₆ and R₁₇ are not both methoxy or ethoxy;

or R₁₆ and R₁₇ together form an oxo (=O) group;

or a pharmaceutically acceptable salt of such compound.

3. (Amended) A compound according to claim 2 wherein B is $-NR_1R_2$, $-NHCHR_1R_2$, $-SCHR_1R_2$ or $-OCHR_1R_2$; R_1 is C_1-C_6 hydrocarbyl, which may optionally be substituted with one hydroxy, fluoro, CF_3 , or C_1-C_2 alkoxy group and may optionally contain one double or triple bond; and R_2 is benzyl or C_1-C_6 hydrocarbyl which may optionally contain one carbon-carbon double or triple bond, wherein said C_1-C_6 alkyl or the phenyl moiety of said benzyl may optionally be substituted with fluoro, CF_3 , C_1-C_2 alkyl, or C_1-C_2 alkoxy.

4. (Amended) A compound according to claim 2 wherein R_1 is C_1-C_6 hydrocarbyl which may be substituted by fluoro, CF_3 , hydroxy, C_1-C_2 alkyl or C_1-C_2 alkoxy and which may optionally contain one carbon-carbon double or triple bond.

14. (Amended) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as gastrointestinal diseases; eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

15. A pharmaceutical composition according to claim 14 for the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders such as depression; and postpartum depression; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections;

neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal, including a human.

Please cancel claims 16-28 without prejudice to the applicants right to file one or more divisional or continuation applications to the subject matter of these claims.

Please add new claims 29 - 40 as follows

- Sub B3*
29. A compound as claimed in claim 1 wherein R24 and R25 are selected from -CF_3 , -CHF_2 , CF_2CF_3 , and CH_2CF_3 .
30. A pharmaceutical composition as claimed in claim 14 for treatment of a mood disorder selected from the group consisting of rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies.
31. A pharmaceutical composition as claimed in claim 14 for treatment of an inflammatory disorder selected from the group consisting of rheumatoid arthritis and osteoarthritis.
- Sub B4*
32. A pharmaceutical composition as claimed in claim 14 for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, child abuse induced depression.
33. A pharmaceutical composition as claimed in claim 14 for treatment of neurodegenerative diseases selected from the group consisting of Alzheimer's disease, Parkinson's disease and Huntington's disease.
34. A pharmaceutical composition as claimed in claim 14 for treatment of chemical dependencies or addictions, selected from the group consisting of dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs.
35. A pharmaceutical composition as claimed in claim 14 for treatment of cerebral ischemia.
- 24 Sub B5*
36. A pharmaceutical composition as claimed in claim 14 for treatment of stress induced immune dysfunctions selected from the group consisting of including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.
37. A pharmaceutical composition as claimed in claim 14 for treatment of fibromyalgia.
38. A pharmaceutical composition as claimed in claim 14 for treatment of anorexia or bulimia nervosa.